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Technology
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FLUORINE AND DENTAL HEALTH

Only two per cent of the population of the United States has entirely escaped the miseries of toothache or the annoyance of the dentist's drill in the filling of a cavity. These difficulties, however, are not peculiar to present-day America. Anthropologists have been able to trace the occurrence of cavities and other dental defects back to prehistoric times; mummies have been found showing dental defects as well as evidences of dental treatment; and written records of dental disease and methods of treatment have been found dating back to 3700 B.C. (1). Dental caries or tooth decay is by far the most prevalent of dental diseases and indeed the most common disease of mankind.

It is surprising, in view of its prevalence, that the ultimate causes of dental caries have remained essentially a mystery. Many theories, however, have been advanced in explanation of caries. Faulty diet, inheritance, neglect of oral hygiene, chemical character of the saliva, bacterial fermentation, and acidity of the oral cavity have at various times been blamed. It is probable that an interplay of all of these is involved in the disease. Of the nutritional factors, calcium, phosphorus, vitamins A, D, and C have been proven essential for the development of sound teeth. Recent research has indicated, however, that although all of these nutritional factors are necessary to strong healthy teeth, their ample provision does not necessarily insure freedom from caries.

Scientific investigations have now revealed the importance of a trace element, *fluorine,* in maintaining teeth which not only are strong, but in addition, are actively resistant to the development of caries. This discovery arose as a result of investigations of an unusual tooth defect, mottled enamel, caused by the ingestion of excessive amounts of fluorine in certain drinking waters. These studies led to the remarkable revelation that although excess fluorine may prove harmful to teeth, smaller optimum amounts of this element are apparently essential to healthy teeth and to the effective inhibition of dental caries.

Because only trace amounts of fluorine are involved both in the production of mottled enamel and in the development of caries-resistant teeth, fluorine control of caries depends upon careful discrimination between beneficial and harmful levels of fluorine in the diet. The recent finding that fluid whole

milk, evaporated milk, skim milk, and other milk products naturally supply valuable trace amounts of fluorine, but which are far below those levels known to produce mottling, is of great significance in the light of the newly recognized role of fluorine in dental health.

The Phenomenon of Mottled Teeth

The story of fluorine and its physiological effect on teeth began less than forty years ago in the Rocky Mountain regions of the United States. A peculiar condition of the teeth of persons living in these sections had been noted for a long time. The unusual tooth condition was characterized by mottling of the enamel with white, chalky patches and discolorations ranging from yellow to dark brown.

In 1908, investigations were initiated in Colorado to determine the cause and nature of this unusual condition. Except for a brief reference by Eager of the U. S. Marine Service in 1902 to an apparently similar condition existing near Naples, Italy, nothing whatsoever had appeared in scientific literature which would serve as a clue for explaining the abnormality. The Colorado investigators, headed by McKay (2), began their search for the cause of mottled teeth by making a general survey of the population in their community. According to their observations:

1. The dental lesions seemed to be confined to children and young adults.

2. Only those children born in the community or who had lived there from early infancy, developed the condition.

3. Children born elsewhere and who subsequently established residence in the community during the period of enamel calcification of certain teeth, developed the lesion on those teeth and on all teeth later calcified in the community; *but those teeth which had been calcified before the child established residence in the afflicted community were entirely normal and remained so.*

From these observations it was apparent that the cause of mottled enamel was localized in particular communities and that the causative effects were exerted only during the period of enamel calcification. Extensive surveys of school children in outlying districts were conducted in an attempt to establish the geographical boundaries of the afflicted area. The studies indicated that the children in the various areas had similar nutritional backgrounds, like exposure to fresh air and sunlight, and other generally consistent environmental conditions. One notable observation was that of two communities only a few miles apart; one exhibited 100 per cent affliction of its native children while the other was completely immune. The two communities, although so close, derived their drinking water from entirely different sources. This difference apparently was the determining factor accounting for the affliction in one town and the complete freedom from the disturbance in the other town only a few miles distant.

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With this single clue, intensive investigations of various water supplies were instituted. Notwithstanding overwhelming circumstantial evidence that certain water supplies carried the factor causing mottled teeth, ordinary chemical analyses did not reveal any significant compositional differences in the various water supplies. At this juncture the situation appeared almost hopeless, for although it was quite certain the cause of mottled enamel resided in the drinking water, attempts to discover the responsible ingredients were fruitless. One fact, however, remained significant—all the waters responsible for the development of mottled enamel came from deep wells or warm springs whereas the waters in non-afflicted communities were usually from cold springs. This differentiation served as the basis for a plan of experimentation involving entire communities. The inhabitants of afflicted communities were induced to change their source of water supply to cold springs or other sources similar to those used by non-afflicted communities. The results, available only after a period of about eight years (the time necessary for permanent teeth to calcify) were indeed gratifying. Mottled enamel had disappeared with the change in drinking water. Further surveys led to the discovery that other communities which had for one reason or another changed to water from deep well sources, experienced the endemic dental defect for the first time. Although the causative agent inherent in certain waters still remained a mystery, all doubt as to the carrier was dispelled.

The first paper in dental literature describing the histopathology involving the tooth enamel and defining the geographical occurrence of endemic "mottled teeth" appeared in 1916 under the authorship of Black and McKay (3).

Excessive Fluorine the Cause of Mottled Enamel

Nearly 25 years elapsed since the early chemical analyses failed to distinguish between ordinary and endemic waters, before spectrographic analyses revealed the presence of traces of fluorine in the waters causing mottled enamel. Samples of water from endemic regions showed from 2 to 14 parts fluorine per million, whereas waters from non-afflicted regions revealed only a fraction of that amount (4). This led to the postulation that fluorine might be the long-sought factor involved in the production of mottled enamel.

Coincident with this new data, Smith, Lantz & Smith engaging in an intensive survey of mottled enamel in St. David, Arizona, likewise came to the conclusion that the unknown cause of the disease probably resided in the water supply (5). These investigators, nutrition chemists at the Arizona Agricultural Experiment Station, undertook to identify the unknown factor in the water by animal experimentation. Animals fed a normal diet to which were added concentrates of drinking water from endemic sections, exhibited unusual changes in the teeth similar to those observed in human mottled enamel. The tooth defects developed under these experimental conditions were so strikingly

similar to those recorded by McCollum et al (6) as a result of feeding fluorides to animals, that the relation between fluorine and mottled teeth immediately became apparent (7).

Further studies confirmed the fact that a positive correlation exists between the fluorine content of food and drink and the development of mottled enamel. With the positive identification of fluorine as the cause of human mottled enamel, new impetus was given to the study and control of this disease. It was then scarcely suspected, however, that such studies would bring to light an even more astonishing discovery, namely, that fluorine in amounts smaller than those causing mottled enamel was apparently essential for good tooth structure actively resistant to dental caries or tooth decay.

Non-Toxic Trace Amounts of Fluorine Prevent Dental Caries

Long before fluorine was identified as the factor in drinking water responsible for mottled enamel, investigators in the field became increasingly aware of an unusual relation between mottled enamel and the incidence of dental caries. Results of numerous surveys disclosed the striking fact that the teeth of individuals with mottled enamel were remarkably free from the usual decay or caries occurring in non-afflicted areas (8).

As studies of the incidence and scope of mottled enamel disease increased, the conviction became established that not only are mottled teeth less susceptible to decay, but that such teeth actively resist decay. The results of three different types of investigation substantiate this conclusion.

Field Surveys: With recognition of fluorine as the causative agent in the development of mottled enamel (dental fluorosis), work was directed toward correlation of fluorine intake, development of mottled enamel and incidence of caries. A series of epidemiological surveys in several endemic areas was conducted by Dean and co-workers of the United States Public Health Service. Public health reports describing their findings indicate conclusively that the greater the fluorine content of the drinking water with resultant mottling of the enamel, the less the incidence of dental decay (9, 10, 11). Further investigations were made to determine the minimal amount of fluorine in drinking water necessary to impart caries-inhibiting properties without causing mottled enamel. Dean and Elvolve found from extensive examination of water supplies that fluorine in concentrations less than one part of fluorine per million parts of water did not produce mottling (12, 13). They later concluded (Dean, Jay, Arnold and Elvolve) that fluorine in concentrations of about 1 part or somewhat less per million prevented caries to an appreciable extent without causing mottling of the enamel (14).

Analytical Studies of Teeth: Field surveys by McKay, Dean and others showing a decrease in incidence of caries in areas of endemic dental fluorosis as well as in regions where the fluorine content of water is high, irrespective of

whether or not the teeth are mottled, are paralleled by actual analytical comparisons of the fluorine content of normal and carious teeth. Chemical analysis of the enamel of sound and carious teeth by Armstrong and Brekhus (15, 16) revealed compositional differences only in the fluorine content; the percentage of gross components, calcium, phosphorus, magnesium and carbonate, were practically identical (Table I). An appreciable difference, however, was found with respect to fluorine content, analyses revealing that sound teeth had a higher fluorine content than did carious teeth (Table II). Even in the same person sound enamel contained approximately 40 per cent more fluorine than carious enamel. Statistical analysis of the results indicated less than one chance in 5,000,000 that the association of the higher amounts of fluorine with the sound teeth was not merely accidental.

Table I. Gross Composition of Enamel of Sound and Carious Teeth*

	Enamel-Sound Teeth			*Enamel-Carious Teeth*		
	Mean	Standard Deviation	Number of Analyses	Mean	Standard Deviation	Number of Analyses
	%	%		%	%	
Calcium	35.35	0.977	43	35.63	0.638	15
Phosphorus	17.43	0.360	43	17.21	0.145	15
Magnesium	0.30	0.041	34	0.32	0.026	15
Carbonate	3.00	0.187	41	3.01	0.129	14

*Armstrong, W. D.—Fluorine and Dental Health. Amer. Assoc. Advancement of Science, Wash., D.C., 1942.

Table II. Fluorine Content of Enamel of Sound and Carious Teeth*

	Mean Fluorine Content	Standard Deviation	Number of Analyses
	%	%	
Enamel-sound teeth	0.0111	0.0020	50
Enamel-carious teeth	0.0069	0.0011	50

*Armstrong, W. D. and Brekhus, P. J. Dent. Res. *17*, 393 (1938)

These studies by Armstrong and Brekhus of human enamel represented the first conclusive evidence that a positive relationship exists between the fluorine content of enamel and the resistance of teeth to dental caries.

Biological Studies with Animals: Still another approach to the fluorine-caries relationship was through experimentation with laboratory animals. Miller in 1938 showed that experimentally induced caries in rats could be prevented almost entirely by the addition of appropriate non-toxic trace amounts of sodium and calcium fluoride to the diet (17). Although the mechanism of fluorine activity in the reduction of dental caries is still problematical, the fact remains that fluorine is effective in inhibiting caries.

The work of Miller in preventing caries in rats by fluorides in the diet has been confirmed by Hodge and Finn (18, 19), and McClure and Arnold (20).

It was further found by Cox and co-workers that not only does fluorine directly inhibit caries, but caries resistance can apparently be "built into the enamel" of offspring by fluorine in the diet of the mother. This hypothesis was reached as a result of animal experiments in which the offspring of mothers fed fluorine during pregnancy and lactation developed decidedly less caries than the animals from mothers not supplied with adequate fluorine (21).

Mechanism of Fluorine Activity In Inhibition of Dental Caries

Dental caries is generally considered to be caused by local disintegration of the tooth substance due to acids produced by bacterial action on food material in the immediate environment of the tooth. Many explanations have been propounded on how fluorine acts in the prevention of dental caries. These theories fall into several broad classifications which are, however, not too widely divergent from each other. McClendon and others (22) suggest that fluorine serves as a building-stone of the enamel and may be an essential to good teeth as are certain vitamins, calcium and phosphorus.

In support of this view McClendon cites the findings of Armstrong and Brekhus (16) that sound teeth contain more fluorine than carious teeth; the experimental results of Cox *et al* (21) that fluorine fed to mothers seems to inhibit caries in the offspring; and the observations of epidemiological surveys by Dean, Jay, Arnold and Elvolve (11, 14) that children who for several years after birth drank water of high fluorine content and then for 12 years drank "fluorine-free" water had less caries than children who drank the same "fluorine-free" water from birth.

Other investigators believe fluorine may increase the acid-resistance of teeth by decreasing their solubility. The work of Volker and others comparing the solubility of normal and fluorosed enamel (enamel with high fluorine content) substantiates this view. Volker reported (23, 24) that fluorine apparently reacts with the tooth substance to form a less soluble product. He postulated that the subsequent decrease in caries may be due to lessened acid-solubility of the teeth due to the incorporation of fluorine in the dental tissues.

It has also been suggested that fluorine, as contained in natural waters, but in amounts insufficient to induce mottling, may act also as an enzyme-inhibitor preventing fermentation of carbohydrate residues in the mouth. Such decomposition of carbohydrate is thought to lead to production of decay-inducing acids. The direct inhibition of acid-producing oral bacteria by fluorine has also been advanced as a further possible explanation for the caries-inhibiting influence of this element.

In addition to the preceding theories much speculation exists on how fluorine is incorporated into the tooth structure. Certain evidence favors the hy-

pothesis that fluorine is adsorbed directly onto the enamel during the passage of fluorine-containing foods or water through the mouth, rather than by systemic absorption and diffusion via the blood stream into the dental tissues. The work of Perry and Armstrong (25) and of Volker, Hodge and associates (26) has contributed much to this phase of the research. However, it is difficult to reconcile this hypothesis with the observations of Cox (21) regarding the favorable influence on the young induced by the fluorine content of the maternal diet.

Whatever the mechanism of the caries inhibiting process by fluorine may be, it is interesting to note that the generally accepted ideas on the cause of caries are not controverted by the new knowledge involving fluorine, nor is the evidence with respect to secondary or predisposing factors involved in tooth decay disputed by the positive evidence concerning fluorine.

Occurrence of Fluorine in Milk and Relation to Incidence of Dental Caries

The influence of fluorine upon tooth structure has been extended to include investigations on the fluorine content of foods. The available evidence indicates that fluorine in foods exerts the same physiological effects on teeth as fluorine in water. This is supported by experiments of McClure (27) on laboratory animals fed fluorine—containing water and foods containing fluorine as sodium fluoride. The importance of milk in the dietary of the young, particularly during the period of calcification of the permanent tooth structure, naturally focuses interest in its fluorine content and the amounts of this important tooth building element which may be contributed by milk. Phillips, Hart and Bohstedt (29) have reported the normal fluorine content of milk to vary between about 0.05 to 0.25 parts per million. These investigators further report that these levels are not significantly increased by feeding relatively high fluorine supplements to cattle*. This wholly removes any possible concern that the inherent fluorine content of milk may be sufficiently high to cause mottled enamel. The fluorine content of milk is well below the amount of at least 1 part per million or more in food or water which must be ingested over long periods before mottling of the teeth makes its appearance.

A recent paper by McClendon, Foster and Supplee (22) records the inherent fluorine content of fluid whole milk, evaporated milk and skim milk produced in various localities of the United States and Canada. Values from 0.04 to 0.44 parts per million were found; the highest individual and average values were found in states south of the 40th parallel, Texas, Mississippi, Tennessee,

*The question has often been raised as to whether cattle or other animals may ingest toxic amounts of fluorine by feeding on certain plants. This question has been answered by the work of MacIntire and co-workers published this December (30). They observed that superphosphate and slag fertilizers containing fluorine failed to affect adversely plants grown on soil treated with these materials and concluded that fluorine in fertilizers does not increase the content of this element in forage crops to any dangerous degree. Accordingly, it is safe to assume that livestock suffer no ill effects from such forage crop feeds.

and Arizona. Their analytical data correlated statistically with the incidence of dental caries in school children, as reported in previous government surveys, led to the conclusion that — "Dental caries in city school children varies inversely with the fluorine content of cows' milk. The correlation coefficient is —0.37." The average number of caries per 100 children 12 to 14 years old in cities south of the 40th parallel was 327 and north of this parallel 473. The average fluorine content of the various milks for these regions was 0.17 p.p.m. and 0.12 p.p.m., respectively.

Additional evidence on the effectiveness of fluorine in food is described in reports on the unusual freedom from dental decay in populations of various islands in the South Seas and the South Atlantic, especially the Island of Tristan da Cunha. Analysis of tooth enamel of natives of this island reveals a high concentration of fluorine (28). The drinking water of Tristan da Cunha contains no fluorine and the source of fluorine has been attributed to the unusually high proportion of fish in the native dietary.

At the present writing, the practical application of caries control by the use of fluorine has already begun. Cheyne (31) reports successful clinical treatment for children, 4½ to 6 years old. Fluorine treatment in these cases resulted in an appreciable decrease in the development of caries and in marked suppression of carious activity in existing lesions.

Conclusion:

Epidemiological, analytical and biological research has culminated in the seeming establishment of trace amounts of fluorine as a dietary essential for sound, decay-resistant teeth. This may well rank as a classical achievement in nutritional and dental research. The problems inherent in the orderly evolution of present knowledge have been peculiarly complicated because of the development of the mottled enamel defect resulting from too high a fluorine intake. Because the difference between the amounts of fluorine producing mottled teeth and the amounts producing decay-resistant teeth is so small, empirical and promiscuous fluorine fortification of food as a caries-prophylactic measure is neither desirable nor expedient. Adequate fluorine intake appears to be possible through natural foods. It is particularly significant that milk and milk products can contribute an appreciable quota of the fluorine required for caries-resistant teeth during the critical age period up to 8 to 10 years without the danger of toxic fluorosis and mottled enamel.

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NEWS DIGEST

MILK contains another water-soluble nutritional factor which has been found necessary for growth in the guinea pig. Animals maintained on a synthetic diet of casein, sugar, mineral salts, corn oil and the known crystalline vitamins (vitamins A, D, C, E, and B complex: thiamin, riboflavin, nicotinic acid, pantothenic acid, pyridoxin, choline) failed to grow, sickened and died within four weeks. Many also developed stomach ulcers. Addition of yeast and grass juice resulted in slightly better growth, but it was not until milk was also added that significant growth and survival responses resulted. An unknown milk factor is thus indicated in addition to yeast, grass juice and the nutrients of the basal diet. The milk factor appears to be involved also in the prevention of stomach ulcers, this activity being distinct from the ulcer-inhibiting properties of milk proteins. Elimination tests indicate the milk factor is not any of the new growth factors (inositol, *p*-aminobenzoic acid, etc.) nor is it apparently folic acid or biotin. It is water-soluble and is found in the skim and whey fractions of milk.

—1101

VITAMIN A of shortening is retained in large measure in the commercial baking of bread, biscuits and white pound cake, but is lost to some extent in the baking of pie crusts. Tests reveal that in the case of the first three products, from 80 to 100% of the vitamin is retained. Pie crust, which undergoes a more severe baking, retains less, the amount of vitamin A decreasing with the length of baking time. In the case of bread, biscuits and pound cake, vitamin A loss is not dependent upon baking time.

—1102

LABILE METHYL GROUPS supplied by the amino acid methionine and by choline have recently been found to be active in inhibiting dermal infection with vaccinia (cowpox virus) in certain laboratory animals. It is hoped that if the effectiveness of these materials for other viruses and for other species of animals is established by future research, a chemotherapeutical agent effective against virus infection may be discovered among these or related substances. (*Cf. Borden's Review of Nutrition Research, Vol. III, No. 1, October, 1942 for complete discussion of the physiological significance of labile methyl groups*).

—1103

HIGH PROTEIN DIETS containing 38 per cent milk casein have been found to exert favorable protective effects against the development of toxic side reactions accompanying administration of sulfa-drugs. Recent experiments designed to study the effects of high carbohydrate, high fat and high protein diets when sulfanilamide is administered, showed that animals on the high protein diet survived considerably longer than did animals on either of the two other diets or animals on a standard control diet. Animals on the high protein diet also gained weight favorably, looked better and were more active.

—1104

COFFEE STRETCHERS designed to increase coffee rations have made their appearance on the market. A typical product contains specially prepared taffy roasted barley, peas, cocoa shells and chicory and is said to effectively double the coffee ration.

—1105

SYNTHETIC SPICES including cinnamon, mace, nutmeg and ginger are new industrial developments designed to meet the shortage of imported spices. Some of the synthetic spices are prepared from bases of dried processed cereal products to which are added small amounts of flavor compounds. These synthetic spices have general characteristics, taste and aroma similar to those of the corresponding natural spices, cost much less, and may be purchased in any quantity without affecting quotas of natural spices.

—1106

JAN 30

TRANSMETHYLATION, or the biological transfer of labile methyl groups from one compound to another, has now been established as a human metabolic process. This proves once again the value of animal experiments in yielding information directly applicable to man. Because many important processes of metabolism are linked together through the transfer of methyl groups, this newly announced concept of the essential nature of labile methyl groups in nutrition, promises to be of tremendous significance. The final proof indicating that transmethylation occurs in man was obtained as a result of isotope studies on a normal male adult, and emphasizes the practical importance in the diet of rich sources of labile methyl groups such as milk (whole, evaporated, powdered), cream, cheese, ice cream, butter, liver, kidney and eggs.

—1107

ENRICHED BREAD, or white bread restored to whole wheat levels with thiamin, niacin and iron, until recently constituted about two-thirds of the total bread production in the United States, thereby adding materially to the general intake of vitamins and minerals. The thiamin intake of the usual diet has been increased by about 30% through adoption of enriched bread. With the new food order necessitating the use of enriched flour in all commercial white bread, effective January 18, 1943, this percentage will be materially increased.

—1108

NOTE: For further information on any of above items address: *Editor,* Borden's Review of Nutrition Research, 350 Madison Avenue, New York, N. Y.